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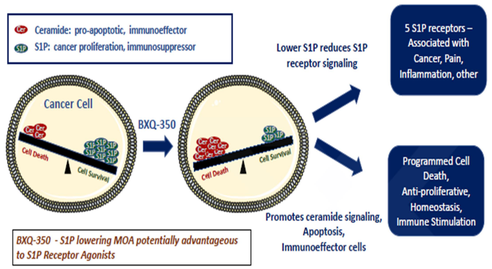
BXQ-350: A Novel Biologic that Modulates Sphingolipid Metabolism and Demonstrates Anti-Cancer, Anti-CIPN, and Anti-Viral Properties

Ray Takigiku, Charlie Cruze, Robin Furnish, Michael Gazda, Tim Stephens, Nikhil Wilkins, Gilles Tapolsky

Bexion Pharmaceuticals, Covington, KY

1. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism

- Normalizes dysregulated sphingolipid metabolism, **lowering S1P and increasing ceramides levels**
- **Modulates S1P signaling & stimulates immune response**

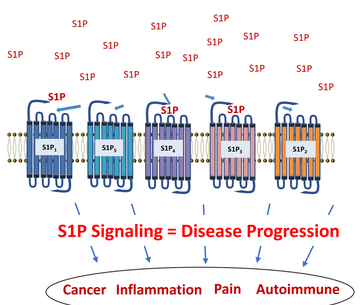


2. Background: Sphingolipids are bioactive signaling molecules implicated in cancer

- **Ceramides** are pro-apoptotic, mitigate resistance and promote an anti-tumoral immune environment
- **Sphingosine-1-phosphate** (S1P) promotes cancer cell proliferation, resistance, oncogenic pathways and a pro-tumoral immune environment
- **Several studies have shown elevated ceramide levels** are associated with **improved survival**

S1P signaling activates multiple oncogenes and induces a pro-tumoral immunosuppressive environment

E.g., see Grbcic, P. et al. *S1P Signaling and Metabolism in Colon Cancer*. Molecules, 2020, 25, 2436.

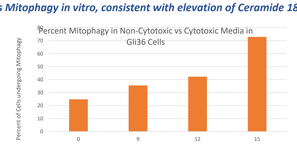


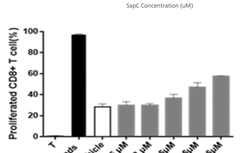
3. Preclinical results, BXQ-350:

a) Increases C18 and lowers S1P across cancer cell lines leading to apoptosis and mitophagy

b) Inhibits MDSCs, expands CD8+ T cells, repolarizes macrophages *ex vivo*

Induces Mitophagy in vitro, consistent with elevation of Ceramide 18





Summary

- **BXQ-350 is a novel biologic** and a nanovesicle formulation of Saposin C, an allosteric activator of enzymes involved in sphingolipid metabolism
- BXQ-350 modulates sphingolipid metabolism**, lowers S1P and increases ceramide levels**
- BXQ-350 **inhibits S1P signaling and rebalances the tumor microenvironment** towards an anti-tumoral state
- In clinical studies, BXQ-350 is **well-tolerated and showed signs of single agent activity in multiple tumor types**
- Investigating systemic levels of S1P and Cer as **potential biomarkers**
- BXQ-350 **may resolve CIPN symptoms in some cancer patients (see CIPN poster)**
- BXQ-350 has **demonstrated activity in vitro across multiple pathogenic viruses**

On-going Studies

Preclinical studies to illustrate BXQ-350's MOA

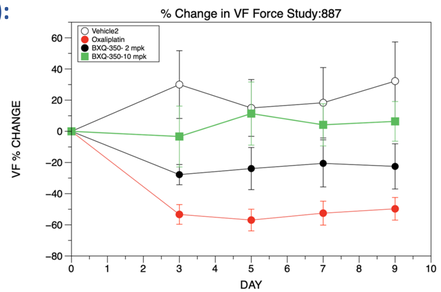
BXQ-350 is clinically being investigated in:

- Phase 1/2 study in combination with SoC in newly diagnosed mCRC patients (NCT05322590)
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)
- Phase 2 study in combination with radiation in pediatric DIPG/Diffuse Midline Glioma patients (NCT04771897)

Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, Bexion's personnel

3. Preclinical results, BXQ-350 (cont):

c. BXQ-350 resolves CIPN symptoms in oxaliplatin-induced preclinical models

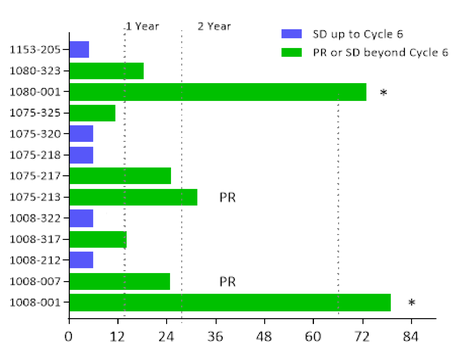


d) BXQ-350 has anti-viral activity due to increasing C18 levels and decreasing S1P

Virus	EC_{50} (µM)	Strain	Host cell
SARS-CoV-2	0.19	KOR/KCDC03/2020	Vero E6 (kidney)
SARS-CoV	4.47	229E HCoV	MRC5 (lung epithelial)
Influenza A H1N1	3.94	California 07/2009	MRC5 (lung epithelial)
RSV	5.41	Long A RSV	MRC5 (lung epithelial)

4. Clinical Results:

- **Phase 1 dose escalation safety study** in all-comer cancer patients with recurrent solid malignancies (NCT02859857) **BXQ-350**
  - **was safe and well-tolerated** (no Dose Limiting Toxicity)
  - **had a 17.8% Clinical Benefit Rate** (CR, PR, SD) at Cycle 6 across tumor types including GBM, brain, CRC, appendiceal, pancreatic and rectal cancers



PFS ≥ 6, 12, 24, 60 months …

- **13 SD / PR patients PFS ≥ Cycle 6** (17.8 % of evaluable pts with clinical benefit) in GBM, CNS, GI and H&N cancers
- **7 patients with PFS ≥ 12 months**

1 GBM and 1 CRC still on study after 6 years